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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/666,511	09/17/2003	Thomas William Rademacher	1012E-910001US	9184

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QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C.
P O BOX 458
ALAMEDA, CA 94501

EXAMINER	
SZPERKA, MICHAEL EDWARD	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 05/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/666,511	RADEMACHER ET AL.	
	Examiner	Art Unit	
	Michael Szperka	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *February 28, 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-33* is/are pending in the application.

4a) Of the above claim(s) *21-22 and 25-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20,23 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/254,800.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/17/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RD

DETAILED ACTION

Applicant's amendment received Feb. 28, 2005 is acknowledged.

Claims 31-33 have been added.

Claims 20-33 are pending in the instant application.

1. Applicant's election with traverse of Group V, claims 23 and 24, drawn to a method of treating obese type II diabetes with an antagonist of A-type IPG in the reply filed on Feb. 28, 2005 is acknowledged. The traversal is on the ground that the restriction is improper since a proper search would encompass all of the inventions, both products and methods, recited in the instant claims. This is not found persuasive because the recited methods of treating diabetes rely on the administration of patentably distinct compositions as part of the method. Further, the disclosed use of one of these patentably distinct compositions to treat diabetes would not anticipate or render obvious the identity, or the methods of using, the other compositions. The examiner does agree with Applicant's argument that a search for methods of using IPG-A inhibitors to treat obese type II diabetes would encompass methods of using IPG-A inhibitors to treat diabetes in general. Therefore, claim 20 (Group III) has been rejoined to the elected group to the extent that it reads on the use of a composition comprising an A-type IPG inhibitor to treat all forms of diabetes. Note that claims 21 and 22 were mistakenly included as part of Group III in the restriction requirement mailed Oct. 21, 2004. Claims 21 and 22 require the composition to contain P- and A- type IPGs, and as such they are properly part of Group I only. The examiner apologizes for the mistake.

However, the separation of Group V, drawn to methods of using A-type IPG inhibitors, and Group X, drawn to a composition containing an antagonist of A-type IPG, is proper, as such a composition could be used to purify A-type IPG or it could be used in methods of treating conditions other than diabetes that would benefit from a reduction in A-type IPG levels. Compositions that contain either different active ingredients, or active ingredients in addition to A-type IPG antagonists, (Groups IX, XI, and XII) will not be examined as these are patentably distinct compositions, as are the methods that use such compositions (Groups I, II, IV, and VII). Note that even though claim 32 is dependent upon claim 23, the composition recited for use in this method claim contains active ingredients in addition to an A-type antagonist, and as such it belongs in Group VI of the restriction requirement mailed Oct. 21, 2004.

The requirement is still deemed proper and is therefore made FINAL.

Claims 21-22 and 25-33 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions. Applicant timely traversed the restriction requirement in the reply filed on Feb. 28, 2005.

Claims 20, 23, and 24 are under examination as they read on methods of treating diabetes with an antagonist of A-type IPGs.

Applicant is reminded to update the first line of specification to indicate that application 09/254,800 has issued as US Patent No. 6,716,592, and to review and update the status of any other applications disclosed in the specification.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 20, 23, and 24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention.

Applicant has claimed a method of treating diabetes by administering an antagonist of an A-type IPG. The specification clearly teaches that there is a correlation between the levels of A- and P-type IPG, the ratio of P- to A-type IPG, and the occurrence of certain forms of diabetes and obesity (see particularly page 6, lines 6-9 of the instant specification). The specification does not teach that alterations in the level of A-type IPG (or the ratio of P- to A-type) causes diabetes, nor is data provided that demonstrates a therapeutic benefit of administering an antagonist of A-type IPG. The specification teaches that antagonists of A-type IPG have one or more of the following

properties: inhibiting the release of A-type IPG, reducing the levels of an A-type IPG, or reducing the effects of an A-type IPG (see particularly page 13, lines 15-25). Specifically recited embodiments of antagonists are naturally occurring binding proteins, antibodies, and synthetic compounds (see particularly page 13; lines 26-32 and page 17, lines 1-15). No examples of naturally occurring binding proteins or synthetic compounds are provided, but Applicant does indicate the generation of polyclonal sera and three monoclonal antibodies (see particularly page 17, lines 33-34). No working examples concerning the administration of the antibodies generated by Applicant, or the administration of A-type IPG antagonists in general, for the treatment of diabetes are provided. Guidance concerning the administration A-type IPG antagonists is minimal, simply indicating that the antagonist is to be administered in an appropriate amount to meet the needs of the individual patient (see particularly page 7, lines 13-16). The administration of antagonists of A-type IPG to diabetic patients is not an art recognized treatment for diabetes (The Merck Manual of Diagnosis and Therapy, pages 165-171, of record as citation 1 on the IDS received Feb. 17, 2004).

Some of Applicant's preferred A-type IPG antagonists are naturally occurring A-type IPG binding molecules. Jones et al. teach that naturally occurring receptors for IPG have not been identified (Int. J. Biochem. And Cell Biol., 1998, 30:313-326, see entire document, particularly the last full sentence of the right column of page 317). Applicant has also indicated that synthetic compounds can be used as antagonists of A-type IPG. While Applicant has disclosed the functional characteristic of A-type IPG antagonists and has disclosed methods to screen compounds for antagonist activity, the

structure of the starting materials used in such screening assays is not disclosed. As such, the specification does not teach a skilled artisan how to make antagonists of A-type IPG that are anything other than antibodies.

Other preferred A-type IPG antagonists are antibodies (see particularly from page 13, line 30 to page 16, line 37 and from page 17, line 18 to page 18, line 35). Applicant has generated antibodies by immunizing animals with IPG purified from rat liver (see particularly page 17, lines 18-19). The immunizing material is not further identified, so it is unclear if the IPG is A-type, P-type, a mixture of both, or some other type of IPG. Jones et al. teach that the structure of IPG is not known, and that all the components of each type of IPG remain unidentified (see particularly the first sentence of the paragraph that spans pages 320 and 321, and the first paragraph of section 7, Directions for future research). Galasko et al. teach that an IPG type different from A- and P-type IPG can be obtained from human plasma (J. Clin. Endocrinol. And Metabolism, 1995, 80:2419-2429, see entire document, particularly the paragraph that spans pages 2426 and 2427). Elased et al. teach that A-type IPG isolated from other organisms, such as *Plasmodium yoelii,* has a different structure than A-type IPG obtained from mammals (Molecular Genetics and Metabolism, 2001, 73:248-258, see entire document, particularly the first full paragraph of the left column of page 256). As such, it is clear that the structure of A-type IPG varies with the source from which the material was obtained, and that the structure of A-type IPG, or the structure of IPG molecules in general, from any source, is not precisely known. Given that Applicant has not disclosed the use of any of the generated antibodies in methods of treatment, or

even that the generated antibodies bind A-type IPG (whatever that structure may be since it varies among species), it is not clear that Applicant's antibodies have any of the properties of A-type IPG antagonists taught by Applicant. It is noted that the specification indicates that all the generated antibodies specifically react with the immunizing antigen, but since the structure of the immunizing antigen is uncertain, as explained above, such a disclosure does not teach the binding specificity of the generated antibodies, specifically that they bind A-type IPG.

Further, it is unclear that an antagonist of A-type IPG would be effective in treating diabetes. Elased et al. teach that the administration of A-type IPG, not an antagonist of A-type IPG, is effective in treating diabetes, as measured by a rapid and significant drop in blood glucose levels (see entire document, particularly the results section, the first complete sentence of the text of the right column of page 255, and the final paragraph of the right column of page 256). This effect was observed in two diabetic model systems, the streptozotocin-induced model of insulin-dependent diabetes and the C57BL/6J-*ob/ob* obese type II diabetic mouse model (see particularly the Results section on page 252, Figures 1A and 1B). An antagonist would block the activity of A-type IPG, and given the teachings of Elased et al. that the activity of A-type IPG is therapeutically beneficial in treating diabetes, such a blockage would either be detrimental to a patient with diabetes, or at least the administration of the A-type IPG antagonist would not be therapeutically beneficial. It is logically inconsistent that an antagonist of a molecule, and the molecule itself, can both have the same therapeutically beneficial effect in treating the same disease or condition.

Therefore, given the lack of working examples in the specification demonstrating a therapeutic benefit of administration of an antagonist of A-type IPG to a diabetic patient, the lack of guidance or a working example of an antagonist of an A-type IPG, the teachings of the art that the precise structure of IPGs of all types are not known and that these structures vary between organisms, and the art teachings that administration of A-type IPG itself, not an antagonist of A-type IPG, is therapeutically beneficial in treating diabetes, a person of skill in the art would be unable to perform Applicant's claimed method without first performing additional research.

4. Claims 20, 23, and 24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicant has claimed a method of treating diabetes using an antagonist of an A-type IPG. The specification indicates that antagonists can be naturally occurring specific binding proteins, antibodies, or synthetic compounds (see particularly page 13, lines 26-31 and page 17, lines 1-15 of the instant specification). The functional properties of A-type IPG antagonists are defined as one or more of the following: inhibiting the release of A-type IPG, reducing the levels of an A-type IPG, or reducing the effects of an A-type IPG (see particularly page 13, lines 15-25).

For naturally occurring binding proteins and synthetic compounds, guidance for

how to screen for such molecules is provided, but the structures of such molecules are not provided. Jones et al. teach that naturally occurring receptors for IPG have not been identified (Int. J. Biochem. And Cell Biol., 1998, 30:313-326, see entire document, particularly the last full sentence of the right column of page 317). Since the identity of naturally occurring IPG binding proteins is not known in the art after the filing date of the instant application, Applicant is clearly not in possession of such molecules. The structure required of a synthetic compound, either at the start of the screening assay or at the end of the assay, are not disclosed. Nor is it disclosed how the structure of such synthetic compounds gives rise to their functional properties as an antagonist of A-type IPG. The remaining recited embodiments of A-type IPG antagonists are antibodies. Applicant has disclosed that antibodies were generated, but it is not clear if these antibodies have the functional properties of A-type IPG inhibitors.

The disclosure of an antigen fully characterized by its structure, formula, chemical name, physical properties, or deposit in a public depository provides an adequate written description of an antibody claimed by its binding affinity to that antigen. Noelle v. Lederman, 355 F.3d 1343, 1349, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (holding there is a lack of written descriptive support for an antibody defined by its binding affinity to an antigen that itself was not adequately described). Applicant has claimed antibodies that specifically bind A-type IPG, but the structure of the IPG used to generate the polyclonal sear and monoclonal antibodies disclosed by Applicant is uncertain since the disclosure does not indicate the type of IPG purified from rat liver used for immunization. The specification also does not appear to provide a fully

characterized structure of A-type, or any other type, of IPG. The state of the art subsequent to Applicant's disclosure teaches that the structure of IPG types are not precisely known, and that the structure of the same IPG type varies depending upon the organism from which that IPG type is isolated (see particularly page 17, lines 18-19 of the instant specification, Jones et al. (particularly the first sentence of the paragraph that spans pages 320 and 321, and the first paragraph of section 7, Directions for future research), and Elased et al. (particularly the first full paragraph of the left column of page 256). The antibodies generated by Applicant have not been disclosed as possessing the properties of A-type IPG antagonists, and given the uncertainty concerning the structure of any type of IPG, it is not clear that antibodies possessing the functional properties of antagonists of A-type IPG can be produced.

Given the lack of a description of the structure of naturally occurring A-type IPG binding molecules, the lack of a description of the structure and the correlation of said structure to the function of synthetic compounds, and the lack of a description of the structure of the antigen recognized by antibodies that have the functional properties of being an antagonist of A-type IPG, a person of skill in the art would conclude that Applicant was not in possession of the claimed genus A-type IPG inhibitors or of the subgenus of antibodies that are antagonists of A-type IPG. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claim 20 is rejected under 35 U.S.C. 102(b) as being anticipated by Naito et al., US patent No. 4,460,765 (see entire document).

Naito et al. teach that griseolic acid and its salts inhibit the activity of cyclic adenosine monophosphate (cAMP) phosphodiesterase (PDE) (see entire document, particularly the abstract and column 1, lines 18-21). Inhibiting cAMP PDE increases the intracellular level of cAMP and therefore can be used as a treatment for diabetes (see particularly column 1, lines 34-43).

Applicant has defined an antagonist of A-type IPG as having one or more of the following properties: inhibiting the release of A-type IPG, reducing the levels of an A-type IPG, or reducing the effects of an A-type IPG (see particularly page 13, lines 15-25). The specification teaches that some of the physiological effects and activities of A-type IPG are to stimulate the activity of cAMP PDE, to inhibit cAMP dependent protein kinase, and to inhibit adenylate cyclase (see particularly page 10, lines 29-32). As such, the activity of A-type IPG serves to decrease the intracellular levels of cAMP.

Therefore, an antagonist of A-type IPG would be expected to increase intracellular levels of cAMP since the activity of A-type IPG is to decrease intracellular cAMP levels.

Naito et al. teach that griseolic acid increases intracellular cAMP levels and is to be used as a treatment for diabetes. The increase is caused by the ability of griseolic acid to inhibit cAMP PDE, and enzyme that is stimulated by A-type IPG. As such, griseolic acid reduces the effects of A-type IPG and is thus an antagonist of A-type IPG.

Therefore, the prior art anticipates the claimed invention.

7. No claims are allowable.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is 571-272-2934. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael Szperka, Ph.D.
Patent Examiner
Technology Center 1600
April 14, 2005

Patrick J. Nolan, Ph.D.
Primary Examiner
Technology Center 1600